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POLICY BRIEF

Towards an economics policy framework to combat malaria, in an era of insecticide resistance

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Abstract

Malaria causes close to half a million deaths per year, the majority of which are in children under five years of age who live in sub-Saharan Africa. Despite significant progress in reducing malaria deaths in the past fifteen years, there is still a long way to go before universal coverage with key interventions like LLINs and IRS is reached, which is an essential step towards achieving malaria elimination. While severe resource constraints pose a fundamental challenge, growing resistance to insecticides used in LLIN and for IRS exacerbates this issue, and threatens to undermine the significant gains achieved to date. This IPPI Policy Brief draws from economic theory to analyse the case of insecticide resistance. It highlights some fundamental trade-offs brought about by the emergence of resistance to insecticides, as well as the lack of data that is necessary to analyse them. The paper also explores how the concept of market failure is applied in the field of malaria control, and where market inefficiencies have not yet been adequately addressed. Overall, while there is no doubt that significant additional funding is needed to combat malaria and hopefully to move closer to its elimination, there is an urgent need to use sound economic analysis to help develop and strengthen a global rationale for further public investment in malaria vector control and to better take account of insecticide resistance in the prioritisation and deployment of national, in-country programmes.

1. Introduction

While there has been substantial progress in scaling up malaria control in the past few years, most malaria endemic countries have still to reach universal coverage of low cost high impact malaria prevention, diagnosis and treatment interventions. The gains made to date in reducing malaria cases and deaths are potentially fragile for a number of reasons. Despite a significant increase in malaria financing in the past ten to fifteen years, severely constrained health budgets and ever-increasing competition for scarce resources have meant that financing falls short of the total needed to render universal coverage possible, and thus pave the way for eradication. Malaria financing across developing countries, and particularly in sub-Saharan Africa is still heavily reliant on external donor financing, and with domestic financing, raises important questions around the sustainability of existing programmes.

Amongst other important challenges, resistance to insecticides used in malaria control has been growing rapidly and poses a huge challenge to the global health community. Though there has not yet been widespread failure of public health insecticides [1], failing to tackle resistance urgently has potentially disastrous consequences [2], and experts argue that three new classes of public health insecticides are necessary to do so effectively [3]. To this aim the innovative vector control consortium (IVCC) was set up ten years ago to develop new public health insecticides to combat malaria. Initially set up with funding from the Bill and Melinda Gates Foundation (BMGF), it is now supported by other donors including UKAID, USAID and the Swiss Agency for Development and Cooperation, and has led to significant progress in the global effort to combat resistance, several new and reformulated insecticide products are in the final stages of development.

However, the knowledge base on the economics of vector control in an era of resistance to insecticides is relatively scarce, particularly as far as new classes of insecticides are concerned. An overall framework for analysing the advent of resistance and its potential economic consequences is lacking. The aim of this policy brief is to propose some first steps towards developing such a framework. In doing so, the authors hope not only to contribute towards global advocacy efforts to combat malaria, but also lay the foundations for a more systematic and comprehensive approach to resource allocation decision-making for malaria control in an era of resistance.

The paper will start by presenting an overview of malaria and its recent history in section two. Section three discusses the issue of insecticide resistance in more detail, including some of the additional challenges it brings about and ways in which it can be addressed. Critically, this section presents some fundamental trade-offs brought about by resistance, which need to be analysed more systematically and explicitly in the resource allocation process. In doing so, it also highlights some major data gaps in modelling resistance and the costs associated with managing it effectively. The fourth section introduces some key economic concepts which are used to analyse the problem of vector control and insecticide resistance in particular. Some examples of market failure in the area of malaria vector control which carry important consequences for policy decisions are discussed. Critically, we seek to demonstrate that the existence of certain types of market failure in particular provides a strong case for public intervention. We conclude in section five by proposing four components of a broader framework to facilitate decision making for vector control in an era of resistance, including ways in which the global community may think about moving forward to build a stronger investment case for malaria vector control in an era of resistance.

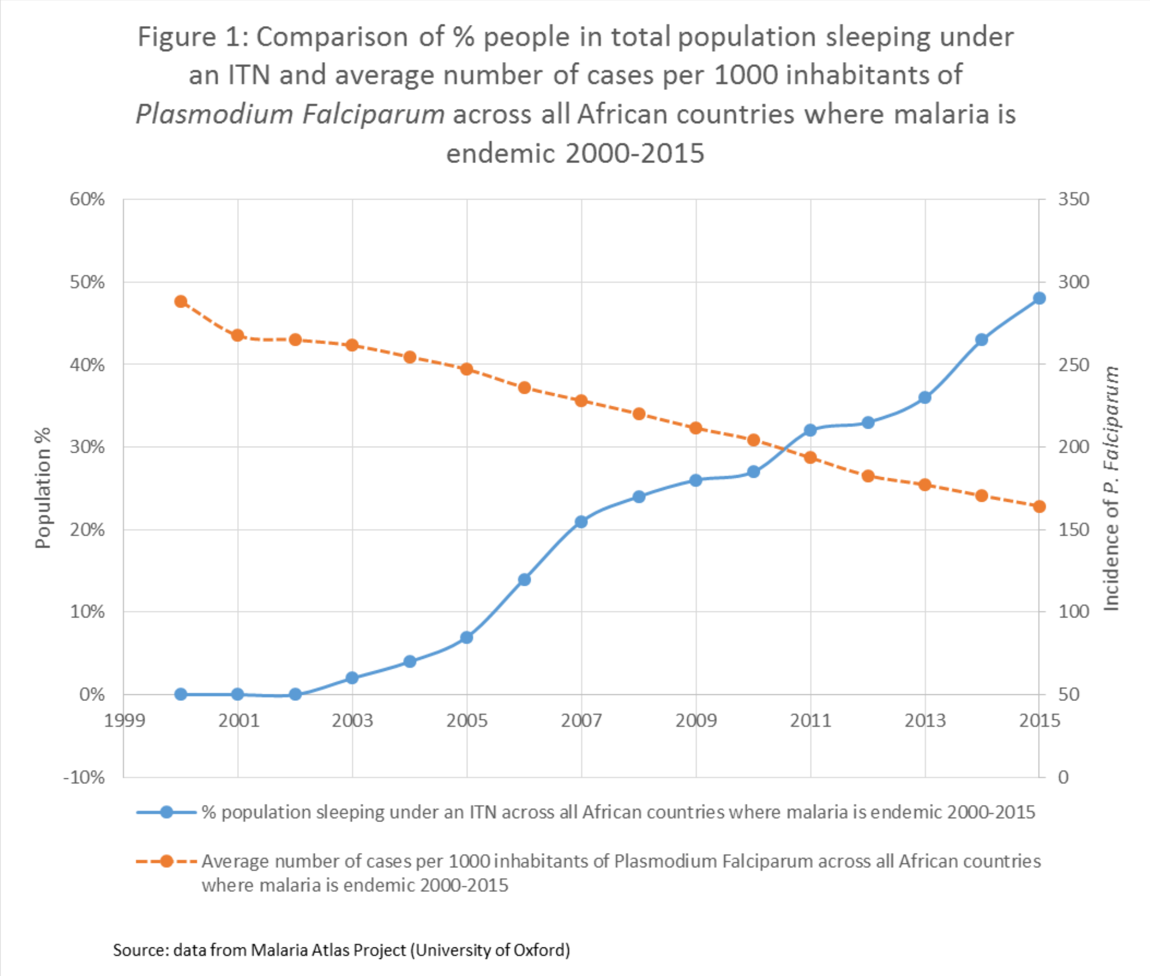
2. Recent history of malaria

Malaria is caused by the Plasmodium parasite, which can be spread to humans through the bites of infected female Anopheles mosquitoes. There are five types of plasmodium parasites that can potentially cause malaria in humans, two of which are currently considered major public health challenges, Plasmodium falciparum and Plasmodium vivax.

Despite being an entirely preventable and treatable disease, 214 million new cases of malaria and 438 000 deaths occurred in 2015 [1]. About 3.2 billion people remain at risk of malaria, and the majority of cases occur in sub-Saharan Africa in children under five years of age. The disease disproportionately affects the poor and disadvantaged for whom the cost of treatment is often unaffordable, placing a huge strain on individuals, families, and society. Though often un-reported, there is also a significant socio-economic impact of lost productivity from prolonged and/or repeated illness [4].

In the past fifteen years, the international community has begun responding to this global health crisis with a dramatic expansion of prevention, treatment and diagnostic interventions, which have resulted in a significant reduction in malaria deaths and incidence rates worldwide. WHO estimates that between 2000 and 2015, the number of malaria cases globally decreased from 262 to 214 million, while deaths from malaria fell by 60% across all age groups, from an estimated 839 000 to 438 000 per year. The proportion of children infected with malaria parasites has been halved in endemic areas of Africa since 2000 [1].

The large scale up of two highly cost-effective vector control interventions, namely indoor residual spraying (IRS) and insecticide treated nets (ITNs) has been a major contributor to this progress. WHO estimates that 49% of the population at risk in sub-Saharan Africa had access to an ITN in their household in 2013 (compared with 3% in 2004), while 44% were sleeping under a net (compared to 2% in 2004) [1]. Figure 1 below compares the dramatic increase in the number of people sleeping under a net since 2000 with the fall in the malaria incidence rate due to Plasmodium falciparum for all African countries where malaria is endemic. Despite a lack of reliable surveillance and other data to measure with certainty the impact of ITNs and IRS across different settings in Africa, a recent study has estimated that mass distribution of ITNs has indeed played a major role in reducing incidence of P falciparum in Africa [5]. Using a large database of malaria field surveys and linking it to detailed reconstructions of changes in intervention coverage, the study estimates that out of an average of 663 million clinical cases averted since 2000, 68% and 10% were due to ITNs and IRS respectively [5]. Thus the authors argue that *"increasing access to potentially l*ife-saving vector control interventions and maintaining their effectiveness in the face of insecticide and drug resistance, should form a cornerstone of post-*2015 control strategies".*



Over the years, malaria control interventions have been shown to be highly cost effective [6, 7] and to yield a high return on investment in public health [8]. Cost per DALY results seen for the distribution of bednets in particular have been comparable to those obtained for administering traditional vaccines, and have tended to be consistently more favourable than those for interventions to combat HIV and TB [9, 10][1]. Furthermore, WHO estimates that reductions in malaria case incidence attributable to malaria control activities are estimated to have saved

[1] While cost per DALY averted has been estimated around $27 (range 8.15-110) and $143 (range 135-150) for ITNs and IRS respectively, the cost per DALY for traditional expanded immunization programmes (EPI) has ranged from $7-$438 per DALY. Meanwhile, results for HIV tend to vary from $0 to infinity, with the majority of results lying above the $150 per DALY benchmark, including most studies which look at anti-retroviral therapy (ART) for mother-to-child prevention. Although the results for TB are complicated by a number of factors, the cost of treating TB (party as a preventive measure) varied from $5 to $50 per DALY. This means that in a country with a high burden of malaria, effective malaria control is likely to be one of the best health sector investments that can be made.

about US$ 900 million on the malaria case management costs in sub-Saharan Africa between 2001 and 2014 [1].

Despite these huge advances, however, there is still a long way to go before universal coverage of malaria prevention is reached, eventually paving the road for malaria elimination, as advocated by the WHO General Technical Strategy for Malaria [8]. One fundamental challenge to achieving these goals is the lack of domestic and international financing. Although global financing for malaria control increased from around US$ 960 million in 2005 to US$ 2.5 billion in 2014, this amount represents less than half of the total amount needed to achieve targets for malaria control and elimination set out in the Global Technical Strategy for Malaria [1]. Worryingly, contributions have grown at a slower pace in recent years, reducing by 8% between 2013 and 2014. With a view to reducing the existing and projected financing gap, WHO has been advocating that malaria endemic countries and donor countries give a higher priority to investments in malaria control.

Furthermore, while the gains achieved are said to be “fragile and unevenly distributed” [8], another major factor which threatens to severely undermine current efforts and even reverse the gains achieved to date, is the occurrence of insecticide resistance to malaria vector control.

3. Insecticide resistance

The rapid scale up of malaria vector control intervention has proved to be a powerful and effective tool to control this potentially deadly disease, yet it has also had some severe unintended negative consequences. As a result of intensified control efforts, the selection pressure on mosquitoes to develop resistance to insecticides used in malaria control has increased dramatically in recent years, and continues to spread rapidly [11]. Mosquito resistance to one or more of the four classes of insecticides currently approved by WHO has been identified in at least 60 malaria-endemic countries worldwide [1]. Resistance continues to spread not only across territories, but also across mosquito species, and in certain cases, fully susceptible mosquito populations are becoming the exception rather than the norm [11].

The problem is particularly severe in the case of ITNs for which only one class of insecticide, the pyrethroids, has been approved for use. In IRS there are more insecticide classes approved for use, however most non-pyrethroids are more expensive or raise other concerns (e.g. environmental impact of DDT) which have made them less attractive to policy makers, implementers and communities in some settings. There are also growing concerns over some mosquito populations which have shown resistance to all four classes of insecticides available for malaria control [11].

The rapid spread of vector resistance to insecticides threatens not only to halt but even reverse the gains recently achieved in malaria vector control [12]. In some countries which have identified and begun to tackle resistance, coverage with IRS has decreased due to use of more costly non-pyrethroid insecticides [12]. Meanwhile, in other countries where resistance is prevalent, pyrethroids are still being used as a single/main insecticide as a result of prohibitive costs of alternative insecticides and limited information on resistance management strategies [12]. This is likely to reduce the effectiveness of IRS. Pyrethroids are the only insecticide class currently approved for use on bednets, meaning that pyrethroid resistance threatens to undermine the public health (transmission reducing) impact of ITNs.

While it is difficult to measure the impact of resistance on the effectiveness of malaria control, WHO and other experts agree there is an urgent need to manage resistance effectively, to avoid reaching a situation where there would be widespread control failure [12]. To this end, WHO has developed a strategy for combating resistance to insecticides, where high priority is given to preserving the susceptibility of major malaria vectors to pyrethroids and other classes of insecticides, and countries are encouraged to implement insecticide resistance management (IRM) strategies where appropriate [12]. The document also notes that short term investment in more expensive IRM strategies is likely to result in longer term cost savings due to extended use of less expensive insecticides.

In this context, some countries have begun to develop and implement insecticide resistance management (IRM) strategies, as a short and medium term solution while new vector control tools are being developed. Current options for IRM are limited but include use of non-pyrethroid IRS and larval source management in combination with standard LLINs. Combination LLINs may also be used as a stop-gap measure while innovative insecticides and new approaches to vector control are developed.

To develop and implement IRM strategies effectively, entomological data concerning each major species should be collected across different settings regularly, in order to track changes over time and follow the most appropriate course of action. Nevertheless, despite the huge investments in ITNs and IRS, many countries do not conduct routine malaria vector surveillance, including for insecticide resistance. According to WHO, among the 97 countries that reported adopting policies for vector control with ITNs or IRS, only 52 reported resistance data for 2014 [1].

The lack of adequate entomological data further exacerbates the challenges posed by the existence of a tipping point, where resistance occurs at a low but gradually increasing level for a number of years, without necessarily being detected. When the tipping point is reached, resistance suddenly increases rapidly and leads to control failure, leaving a limited timeframe within which to act to avoid disastrous consequences. This occurred in Mexico, for example, where the frequency of resistance was very low at most sentinel sites between 2000 and 2003. However at some point between 2003 and 2007, resistance suddenly began to increase rapidly and reached a frequency greater than 80% by 2007. Evidence is building that a number of countries are rapidly approaching a tipping point, and that urgent action is needed [13].

Growing resistance to insecticides for malaria vector control poses major economic and other challenges for policy making at global and national levels, particularly as universal coverage to improve overall population health remains the overarching goal in malaria vector control [1]. Resistance is likely to put even more pressure on already weak health systems and challenge the financial feasibility of malaria elimination, meaning that more resources are needed for malaria control. While new vector control tools are currently being developed that could potentially be effective in tackling resistance and preserving or prolonging susceptibility to insecticides, intense competition for resources and constrained health budgets in general, and for malaria control specifically, mean options in reality are limited.

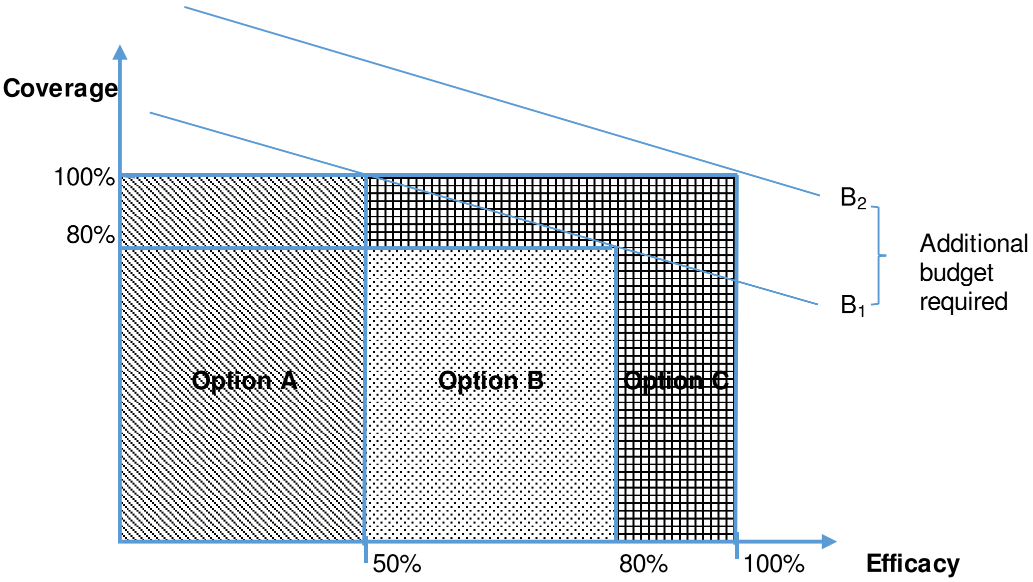
Policy makers will face a difficult time trade-off between coverage, efficacy and cost as illustrated in Figures 2 and 3.

Figure 2 shows the coverage efficacy trade-off forced on policy makers acting under a budget constraint. There is growing evidence of increasing resistance (lower efficacy), leading to reduced programme effectiveness. In some cases, where resistance has been identified and policy makers have begun to invest in tackling it, malaria programmes have opted for alternative, more expensive insecticides and lower coverage [14]. While efficacy of alternative insecticide is higher than that of pyrethroid, it is unlikely to be 100%, particularly in the medium and long term, as resistance to these alternatives is likely to develop. Similarly, attaining 100% coverage is hardly achievable due to a range of challenges, including reaching some of the more remote communities in Africa, as well as ensuring adequate utilisation of bednets [1]. Significant additional investment will be necessary to ensure a high coverage can be achieved at the same time as high efficacy.

Figure 3 demonstrates that the trade-off is complicated by alternative strategies for deployment of multiple insecticides (with different modes of action) and the existence of a tipping point. Three insecticides could either be deployed in combination or sequentially, and the area under the curve for each strategy corresponds to the amount of protective efficacy gained. Theoretically, the combination strategy maintains full efficacy over the course of the programme. While this approach may cost more in the short run, it should result in long term cost savings and efficacy gain [12], avoiding the expense of developing additional new insecticides.

Although figures 2 and 3 show theoretical trade-offs and the potential impact of insecticide resistance over time on programme effectiveness, one fundamental challenge is that we lack data to try and plot what the real trade-offs might look like in practice, including in terms of financial implications. Further modelling that takes account of resistance and its potential path over time, combined with decision tools that are appropriate for each context are necessary to support policy makers in resource allocation decisions to address the challenge of insecticide resistance, particularly in view of the limited time that may be available and severely constrained budgets.

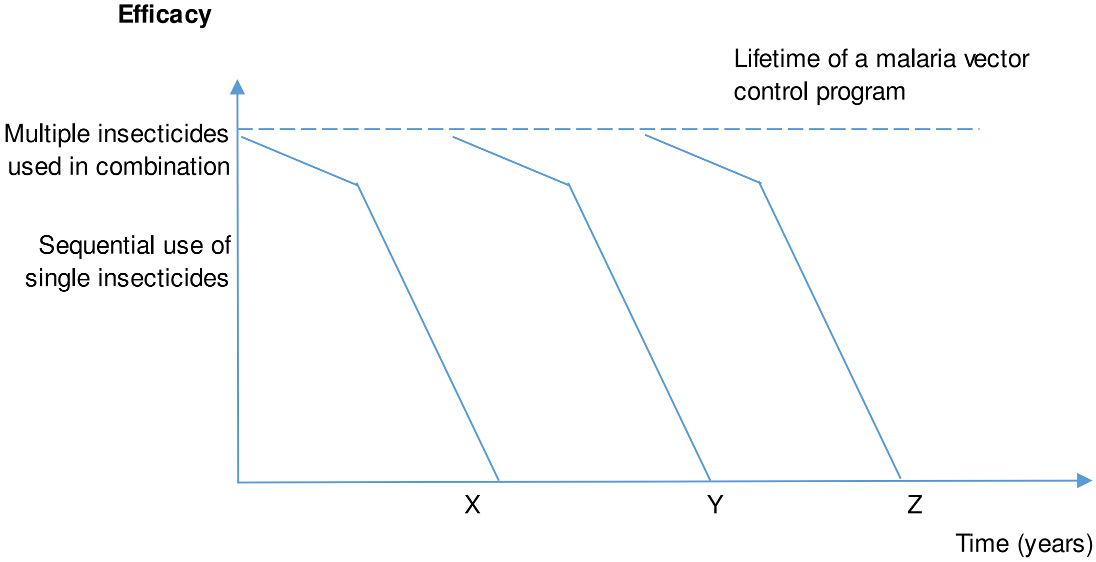
Figure 2: Coverage-efficacy trade-off under a budget constraint



Legend: B_1 Initial budget sufficient to support either A (100% coverage, 50% efficacy) or B (80% coverage, 80% efficacy). Option C (100% coverage, 100% efficacy) possible only with higher budget B_2.

Source: authors

Figure 3: Sequential versus combined use of different insecticides



Legend: Solid line shows efficacy of sequential use of single insecticides. Initially high efficacy declines slowly at first, then reaches a tipping point where it declines steeply. Efficacy is regained by switch to alternative insecticide at time X. The process is repeated at time Y and Z when potentially a forth new insecticide is required, entailing high research and development costs. Dashed line shows theoretical efficacy of a combination of three insecticides with different modes of action used as part of a pro-active resistance management approach. In this strategy, efficacy is maintained for the lifetime of the programme.

Source: authors

4. Vector control and market failure

There are numerous failures in the market for vector control and IRM (Table 1). While a number of market failures are already being tackled on a global scale, the rising problem of insecticide resistance, an externality of large scale ITN distribution programme in the last few years, poses fresh challenges that are only being partially addressed by public policy.

Table 1. Market failures in vector control (VC) and insecticide resistance management (IRM)

Market Failure	Definition	Example in VC and/or IRM	Addressed by public policy?
Missing markets	Markets may fail to form, resulting in a failure to meet a need or want, such as the need for **public goods**. Public goods or services, if they are provided at all, are open to use by all members of society. As such, they are non-excludable and non-rivalrous in that individuals cannot be effectively excluded from use and where use by one individual does not reduce availability to others.	VC: The vector killing effect of insecticides used in IRS and LLIN IRM: The effect of reducing the spread of resistance and thereby prolonging susceptibility to insecticide (if this is done for one setting/country, other settings/countries benefit too, as mosquitoes do not recognize borders). This leads to limited demand for vector control products, particularly more expensive, innovative products. In turn, unless there is public intervention, there is limited research.	Yes via free (sometimes targeted, donor funded) distribution of LLIN and IRS Partially via funding for product development partnerships (PDP) such as IVCC However, action to stimulate the demand for new products remains inadequate
Incomplete markets	Markets may fail to produce enough **merit goods**, which are goods where public benefit is greater than private benefit. Without intervention, this leads to under-consumption.	As above	As above
Negative externality	Negative effect from an activity which does not accrue to the person carrying it out.	Resistance as an externality of vector control	Partially by encouraging countries to strengthen surveillance systems and implement IRM strategies where necessary. However funding is still lacking for this, and many countries are still over-using single insecticides. Limited action has been taken on a global scale to stimulate demand for new (more expensive) insecticides
Positive externality	Positive effect from an activity which does not accrue to the person carrying it out.	VC: Benefits of an individual sleeping under a bednet accrues not only to him/her but also to other members of the community IRM: Benefits of one setting/country implementing IRM strategy benefits neighbouring settings/countries	Partially through promoting multi-country action to combat resistance. However limited funds and lack of adequate coordination mechanisms have stifled steady progress
Non-competitive markets	A market where there are a limited number of sellers.	Limited number of manufacturers of (innovative) vector control products used to manage resistance means that product prices remain extremely high.	Despite encouraging PDP for innovative vector control products, limited action has been taken to ensure end products can be made affordable to their users.

Information asymmetry	Decisions in transactions where one party has more or better information than the other, which creates an imbalance of power.	See below under "principal-agent problem"	
Principal-agent problem	Arises where the two parties have different interests and **asymmetric information** (the agent having more information), such that the principal cannot directly ensure that the agent is always acting in the principal's best interests, particularly when activities that are useful to the principal are costly to the agent, and where elements of what the agent does are costly for the principal to observe.	Policy makers in developing countries (the agents) make decisions on behalf of the population, or voters (the principal). Faced with a limited budget and given pressure to secure votes, governments may have a disincentive to reduce coverage in favour of more effective products, to which resistance is less likely to develop. Donors are sometimes motivated by their own priorities and approaches to resource allocation for vector control and IRM which are not necessarily aligned with recipient countries' priorities (This problem may occur as the international community is seeking to address the principal-agent problem where the government is acting as the agent for the population).	Free (donor funded) vector control programs which are targeted at specific regions or population group (this remedial action constitutes another principal-agent problem in itself between the donor and the recipient government). Increased research capacity in malaria endemic countries to make informed technical choices and greater democratic accountability within civil society.
Time-inconsistent preferences	Decisions being made at different points in time can be inconsistent with each other. This occurs because people can be disproportionately attracted to immediately available rewards. When two rewards are both substantially delayed, the individual is able to make a rational trade-off between them. However, when one reward is imminent, it exerts a disproportionate attraction.	IRM: decision-makers are likely to favour achieving high intervention coverage with current (cheaper) vector control interventions today, and thus unwilling to opt for more effective (and considerably more expensive) interventions, in order to save additional lives in the future.	Assessment of the costs and benefits of decisions over a long time horizon to be used to inform public policy.

Akin to a vaccination campaign (see Box 1), the effect of malaria vector control using insecticides can be considered a **public good** and as such bears some positive externalities to society as a whole. Indeed, vector control is both non-rival (can be consumed by one user without preventing simultaneous consumption by another) and non-excludable (non-paying consumers cannot be prevented from benefitting from it). While IRS is a public good by its nature (the mosquito is killed as it rests on the wall after biting and thus doesn't go on to transmit an infection it may have picked up from that bite), LLINs in particular confer not only private but also public benefits, as

(1) some mosquitos will encounter the insecticide and die, and will not go on to infect other people;

and

(2) insofar as the members of the household have fewer cases of malaria, when they are bitten by mosquitos in the future, these mosquitos will not become infected and cannot pass malaria to other people.

Points (1) and (2) above illustrate that vector control products also display the classic attributes of a **merit good** (see also box 1). Individuals don't take into account the benefits to society as a whole (or positive externalities) of being protected through a bednet or IRS when making decisions.

Box 1. A public and a merit good

Immunization campaigns carry a positive externality. Each person who is vaccinated not only reduces their own chance of contracting the disease against which s/he has been immunized, but also lowers the risk of others in the community becoming ill. However, if vaccination campaigns were not publicly funded, individuals would not have an incentive to pay a higher price for receiving the vaccine which takes into account the benefits to society as a whole, nor would others in the community have an incentive to cover of the cost of their "share" of benefit from someone else being vaccinated. In other words, the latter individuals are said to free ride. The effect of vaccination campaign is thus considered a public good, because even if it is "consumed" by one person, it can still be "consumed" by other people, and individuals are not competing for it. It is also a merit good because individuals do not take into account the benefits to society of being immunized. Partly as a result of inadequate information, they may also under-estimate the benefit of receiving a vaccination. In contrast to a public good, if I eat an ice-cream, no one else can eat it, and the ice-cream is thus a private good.

There is also an informational problem, as inhabitants of a household where nets are used have a tendency to underestimate the private benefit they obtain from using a net appropriately (they are less likely to be bitten by an infectious mosquito and become infected themselves), as they may not fully understand either the dynamics of malaria as a disease or the role of insecticides in preventing malaria. This is partly but not entirely because of lack of education and public health communication – but also because malaria is a stubborn and complex disease, with a tendency to fight back against control efforts.

While public goods may not be produced at all if markets are left to themselves, merit goods are both under-produced and under-consumed in the free market, which forms the basis of the economic argument for public investment in malaria vector control. In other words, limited information about benefits, alongside the existence of the public benefits of insecticidal protection, provide the economic rationale for public authorities (such as donors or governments) stepping in to provide IRS and ITNs to populations living in area of malaria transmission. Global public health authorities have partially responded to these challenges with free large-scale distribution campaigns of LLINs and IRS. More recently, UNITAID has supported a subsidy mechanism to attempt to grow the market for a new long lasting non-pyrethroid chemical for IRS[2].

Market failure in an era of resistance

While the implementation of large-scale vector control programmes has resulted in a dramatic reduction in malaria cases worldwide over the last fifteen years, they have also created a major public disbenefit, or **negative externality** (see box 2). Resistance occurs as a result of selective pressure on malaria vectors through repeated use of single insecticides. Overuse of single insecticides for malaria vector control also creates a negative externality in the control of other vector borne diseases compromising integrated vector management strategies for multiple disease control [12].

Box 2. A negative externality

When a firm emits pollution into the air, this has a negative impact on the environment and on people living nearby who are forced to breathe in polluted air. If the same firm were to invest in technology which reduces pollution, however, everybody in the area would benefit from breathing in fresh air, but nobody would be paying the firm for its investment. This gives rise to a problem which economists call free riding. The firm has thus no incentive to invest in more expensive technology to reduce pollution, unless it is incentivized to do so by the government, either through a subsidy or through taxation on "dirty" emissions.

Experts agree there is an urgency to reduce the use of insecticides (pyrethroid in particular) as mono-therapies to reduce this selective pressure on malaria vectors and thus avoid disastrous consequences of reaching a tipping point before other active ingredients have been developed. When the new active ingredients reach the market they too need to be protected to avoid rapid emergence of resistance. The risk of insecticide resistance to current and new insecticides would be significantly mitigated by deployment of effective IRM strategies. The question then becomes one of how to make this happen in an imperfect market.

Analogous to vector control, the effect of insecticide resistance management (IRM), is a **public and merit good** where the market exhibits significant failures, the costs and benefits of short or long term strategies are borne at different levels as a result of existing externalities. Any country investing in IRM creates a positive externality by reducing the likelihood of resistance spreading locally and in other countries. Yet there is a disincentive for one country to invest in IRM, even if it slows the spread of resistance, because while they bear all the costs, not all the benefits will accrue to them. Thus there is

[2] http://www.ngenirs.org/

a global benefit but the costs are borne out of country budgets, also entailing that countries have an incentive to free ride when their neighbours are already investing in IRM.

The rapid rise of resistance has also meant that the need to incentivize R&D in the field of vector control has become more pressing. The fact that it has been developing so fast and the existence of a potential tipping point has meant that rapid progress is necessary in approving new ingredients for use as public health insecticides in vector control, before all the gains achieved to date are lost.

However, due to their nature as a public and merit good, there is also a lack of knowledge and research for vector control products. The problem is further exacerbated by the fact that people in need of these products are relatively poor and therefore only able to pay a low price for them. Limited demand, high R&D costs and the high risks involved mean that firms have limited incentive to invest in them, thus the need for public intervention. Publicly funded initiatives such as IVCC have been instrumental in promoting effective collaboration amongst experts in the development of new active ingredients. However, despite these efforts to stimulate R&D for new insecticides, limited action has been taken to encourage pro-active resistance management as an immediate measure, stimulate the demand for new Active Ingredients (AIs), and to protect future effectiveness of new AIs currently being developed.

Another important market failure that occurs in the field of vector control and has been exacerbated by the occurrence of resistance is a fundamental economic challenge known as the **principal-agent problem**, which often occurs partially as a result of **information asymmetry**. Within a country, while policy makers (the agent) have more and better information on the benefits of vector control and managing resistance than the population (the principal), their respective incentives may not always be aligned. In particular, policy makers' incentives to achieve high levels of coverage (in order to be seen to protect large proportions of the population) may not always ensure that the poorest or most at risk populations are adequately taken care of. While both IRS and ITN programmes will be more costly for more remote populations, targeted ITN distribution programmes (for example for pregnant women or children under five) may also be more expensive if they require that more than one net per targeted individual to be distributed, in order to reflect the fact that other members of the family will also be using nets [7]. This in turn raises some important questions around how to ensure equity is taken into account when governments have to operate under constrained budgets.

Ironically, the international community's attempt to address the above challenges may give rise to further issues, where international donors act as agents for developing country governments (the principal). In particular, issues are likely to arise when donors fund and manage a series of vector control projects in recipient countries, over which they have almost complete control and primarily reflect donor country priorities. At the same time, while value-for-money may present a useful framework for priority-setting where resources are limited, there may also be some unintended negative consequences. For example, the UK government recommends that funding should be prioritised for settings where coverage rates are still relatively low and malaria mortality remains high [15], in order to maximize the health benefits achieved. While this makes sense from a purely economic perspective, it is also the case that additional resources will be necessary to manage resistance in those countries which have already reached high levels of coverage and reduction in malaria mortality, in order to avoid the potentially catastrophic consequences of resistance to insecticides developing at a faster rate and spreading across territories.

Closely related to the principal-agent problem in the area of IRM in particular, is the fact that decision makers often have **time-inconsistent preferences** (see box 3) [16, 17]. While the extent to which this phenomenon occurs will be dependent on the discount rate the consequences for malaria control and elimination are severe, as actions that should be taken today are unduly delayed. Decision makers operate under a certain degree of political and economic pressure from their own population as well as international donors, and they are aware that their career as a policy maker may be short-lived and highly dependent on immediate results. Given a constrained budget, the choice to reduce coverage today in order to increase effectiveness and eventually save additional lives in the future is near impossible for decision makers on the grounds, as this is likely to cost lives in the short run. Furthermore, reducing coverage in order to choose more effective interventions would mean that coverage targets set by the international community would not be met, thus potentially affecting countries' ability to access further funds to combat malaria.

Box 3. Time-inconsistent preferences

Thinking about the following question:

(a) Which do you prefer, be given 10 pounds today or 12 pounds tomorrow?

(b) Which do you prefer, be given 10 pounds 365 days later or 12 pounds 366 days later?

When this question is asked, to be time-consistent, people must choose "12 pounds tomorrow" for question (a) and "12 pounds 366 days later" for question (b). However, people are not always consistent, and tend to choose "10 pounds today" and "12 pounds 366 days later", which is different from the time-consistent answer. This occurs because people may be disproportionately attracted to short term rewards.

5. Conclusion and recommendations

There is clear global recognition that insecticide resistance represents a major source of concern for the sustainability of current malaria control programmes. Major advances have been made and it would be tragic if the gains which have been made in the last 10-15 years were lost, particularly given malaria eradication is back on the global health agenda. Development partners continue to demonstrate a strong commitment towards malaria control and eradication efforts. The UK and the Bill and Melinda Gates Foundation recently announced US$4.28 billion in funding over the next five years for research and to support efforts to eliminate this disease [18].

In order to ensure that these and further investments in malaria control and eradication achieve the greatest value-for-money impact, we argue that a framework is necessary which can help countries' to strike the balance between advancing towards universal coverage and taking actions to protect already won gains by increases in insecticide resistance, while also looking towards malaria eradication. Such a framework would also help donors identify how best to allocate funds in order to maximize benefits and look at ways in which to ensure sustained financing. While many of the elements of this framework will necessarily draw on medical and entomological science, we focus on the key economic ideas which must underpin such a framework. We propose four main steps towards the creation of this framework.

1. **Explicitly consider trade-offs that arise from resource allocation decisions in malaria vector control, particularly those forced by resistance.** Such trade-offs have the potential to be politically contentious, and include coverage-efficacy as well as time trade-offs illustrated in section two above. They also include the need to balance equity versus efficiency, closely linked to the discussion on market failure arising from information asymmetries and lack of information.

2. **Further develop and promote the use of resource allocation tools for vector control that systematically take account of resistance in different settings.** In order to do so, further modelling of insecticide resistance (analogous to work which has been done for drug resistance) is necessary, that seek to trace the path that resistance is likely to take over the next few years in different settings. As has already been highlighted elsewhere [12], more detailed financial data on insecticide resistance management as well as new tools (including those currently in the development pipeline) are necessary to ensure the analysis is comprehensive. This will enable policy makers in developing countries to access information on a comprehensive set of available options for combating malaria in an era of resistance, and thus not only facilitate the resource allocation process, but also aid the achievement of a fair price setting mechanisms for manufacturers.

3. **Urgently address the global challenge posed by the effect of insecticide resistance management displaying attributes of a public and a merit good.** We argue that this factor alone presents a strong economic basis for a global, multi-sectoral intervention to tackle insecticide resistance. We also suggest that because of the informational problems in assessing the impact of resistance, countries and donors have significantly under-prioritised investing in guarding against insecticide resistance within their malaria control investment portfolios. While efforts have been made to stimulate the supply of innovative tools for vector control, limited action has been taken to generate the necessary additional demand for these products. We therefore suggest that further work is undertaken on the creation of potentially new innovative financing tools for vector control products. We also propose that in-depth global level analysis be undertaken on the value of susceptibility to insecticides used for vector control and the importance of preserving it, drawing from the work already undertaken in the field of anti-malarial drugs where relevant and appropriate [19, 20].

4. **Ensure that existing market failures in malaria vector control in an era of resistance are systematically taken into account in value-for-money analyses and corresponding resource allocation decisions**. This recommendation closely ties in with recommendation 2

and calls for a more comprehensive and flexible approach to resource allocation in malaria vector control. We suggest this would encourage policy makers to systematically consider a range of factors which may be more difficult not only to quantify in financial terms but also to justify politically, but also facilitate the design of adequate solutions to address specific market failures in varying contexts.

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Annex One – Glossary of Terms

(i) Health and malaria terms

Combination LLINs: bednets with two or more active ingredients.

Disease-Adjusted Life Year (DALY): A measure of overall disease burden, expressed as the number of years lost due to ill-health, disability or early death.

Indoor residual spraying (IRS): The process of spraying the inside of dwellings with an insecticide to target indoor biting mosquitoes that spread malaria. Susceptible mosquitoes are killed when they come into contact with the insecticide.

Insecticide-treated net (ITN): A net (usually a bed net), designed to block mosquitoes physically, that has been treated with safe, residual insecticide for the purpose of killing mosquitoes, which carry malaria. To-date, only one insecticide class, the pyrethroids, has been approved for this purpose on bednets.

Long-lasting Insecticide-treated nets (LLIN): An ITN with pyrethroid insecticides incorporated into its fibre and designed to remain effective against susceptible mosquitoes for multiple years without retreatment (usually about three years).

Malaria vector: In epidemiology, a vector is any agent (person, animal, or microorganism) that carries and transmits an infectious pathogen into another living organism. Mosquitos are a vector for several diseases, most notably malaria.

Tipping point: the point at which a series of small changes or incidents becomes significant enough to cause a larger, more important change. In the case of resistance to public health insecticides, a “tipping point” describes the fact that resistance can occur at low but gradually increasing frequency in the vector population for many years without being detected. When a “tipping point” is reached, however, resistance may increase extremely rapidly and becomes detectable within a population, thus becoming operationally significant for malaria control programmes and potentially leading to control failure.

(ii) Economic terms

Externality: A cost or benefit arising from an activity which does not accrue to the person or organization carrying out the activity.

Free riding: When a person or organization benefits from a public good, but neither provides it nor contributes to the cost of collective provision. They thus free ride on the efforts of others.

Incomplete markets: Markets may fail to produce enough merit goods (see below), such as education and healthcare.

Information asymmetry: A situation where one party has more or better information than the other. This creates an imbalance of power in transactions, and may result in individuals making choices which are neither in their best interests, nor that of society.

Market failure: describes a situation where markets, when left to themselves, are not successful at allocating resources efficiently, and hence an intervention by an external party, such as government or other institution may be warranted.

Merit goods: A good which would be under-consumed (and under-produced) in the free market economy, as its consumption generates a positive externality. As a result, the public benefit of consuming a merit good is greater than the private benefit of doing so. As consumers only take into account private benefits when consuming merit goods, they are under-consumed (and so under-produced). In addition, individuals do not tend to taking into account the long term benefits of consuming a merit good and so they are under-consumed.

Missing market: Occurs when markets may fail to form, resulting in a failure to meet a need or want, such as the need for public goods.

Principal-Agent problem: Arises where the two parties have different interests and **asymmetric information** (the agent having more information), such that the principal cannot directly ensure that the agent is always acting in its (the principal's) best interests, particularly when activities that are useful to the principal are costly to the agent, and where elements of what the agent does are costly for the principal to observe.

Public goods: Goods or services which, if they are provided at all, are open to use by all members of society. As such, they are non-excludable and non-rivalrous in that individuals cannot be effectively excluded from use and where use by one individual does not reduce availability to others. As nobody can be excluded from using them, public goods cannot be provided for private profit.

Return on investment: The benefit to the investor resulting from an investment of some resource. A high ROI means the investment gains compare favorably to investment cost.

Time-inconsistent preferences: Decisions being made at different points in time can be inconsistent with each other. In particular, when particular rewards are imminent, they exert a disproportionate attraction.

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